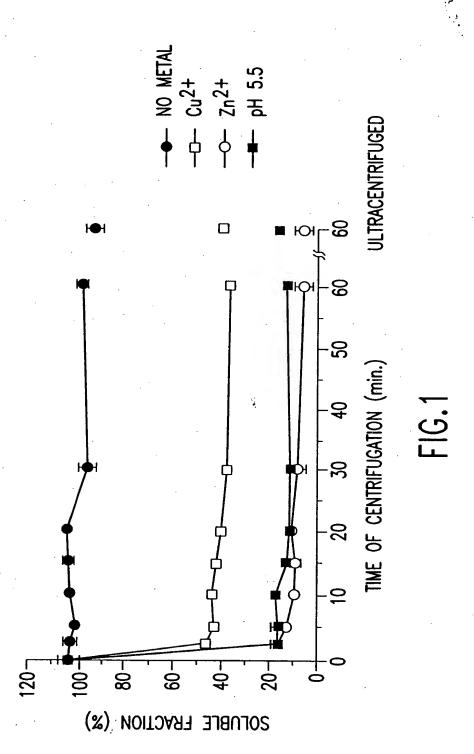
Dkt. No. 0609.4550001/JAG/FRC; Batch No.: N/A Inventor(s): Bush et al.; Tel: 202/371-2600
Title: Agents for Use in the Treatment of Alzheimer's Disease



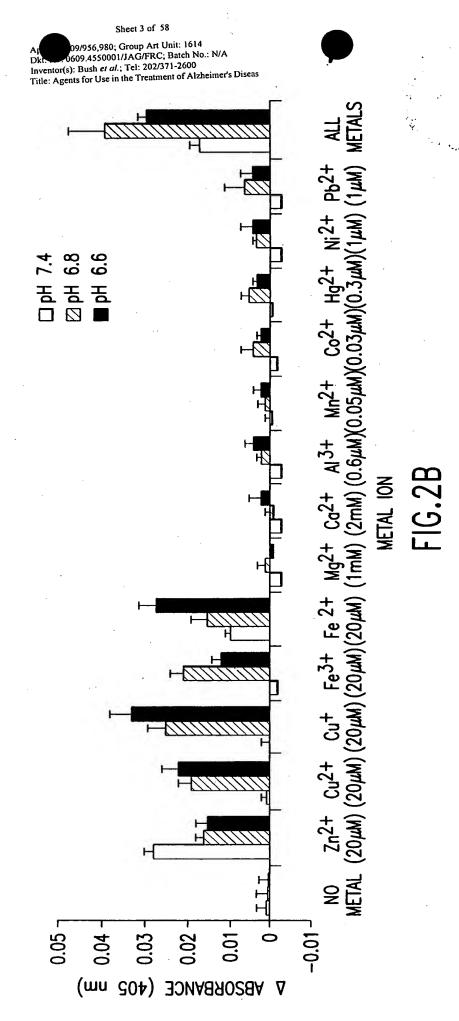


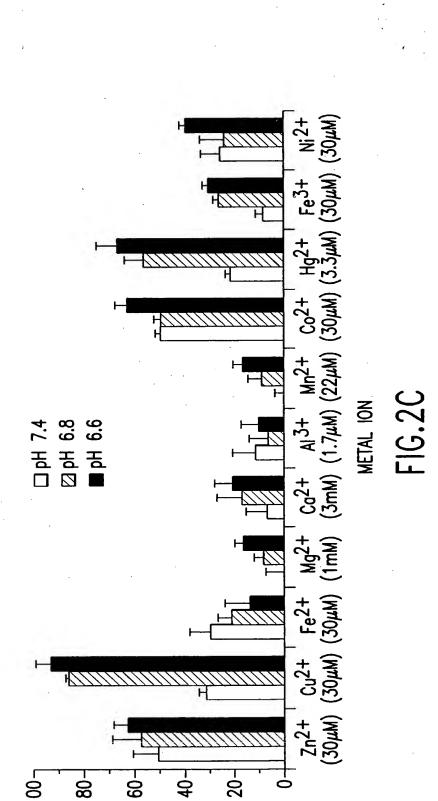
80

-09

% AGGREGATION

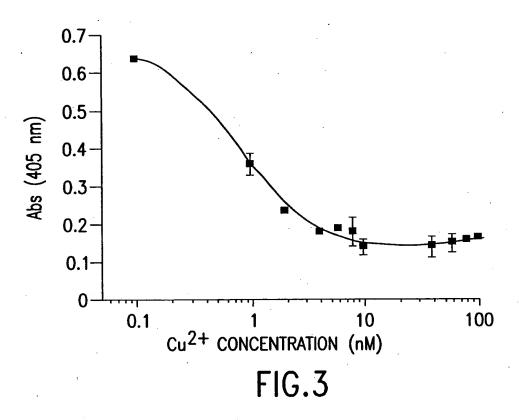
20-

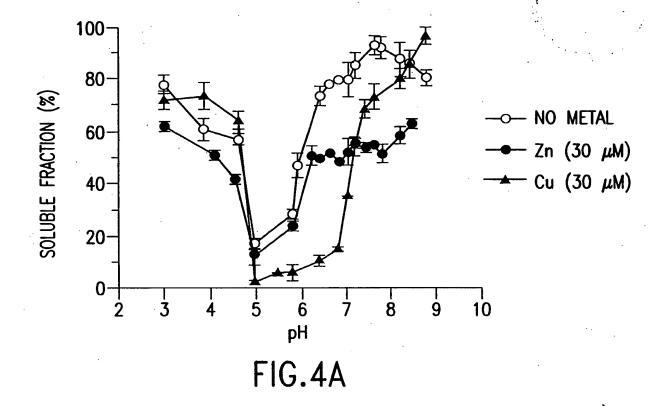


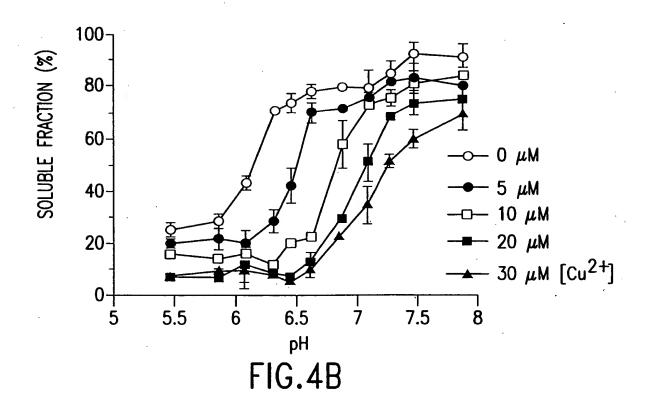


% AGGREAGATION

Sheet 4 of 58







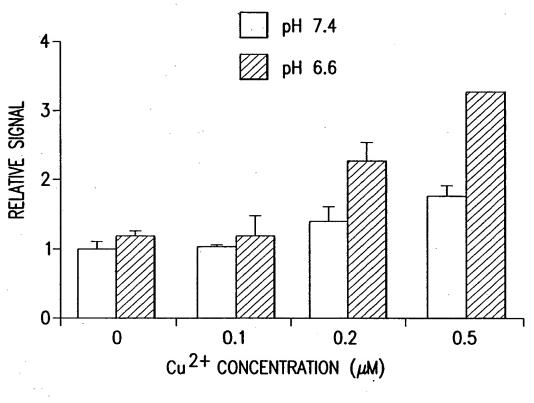
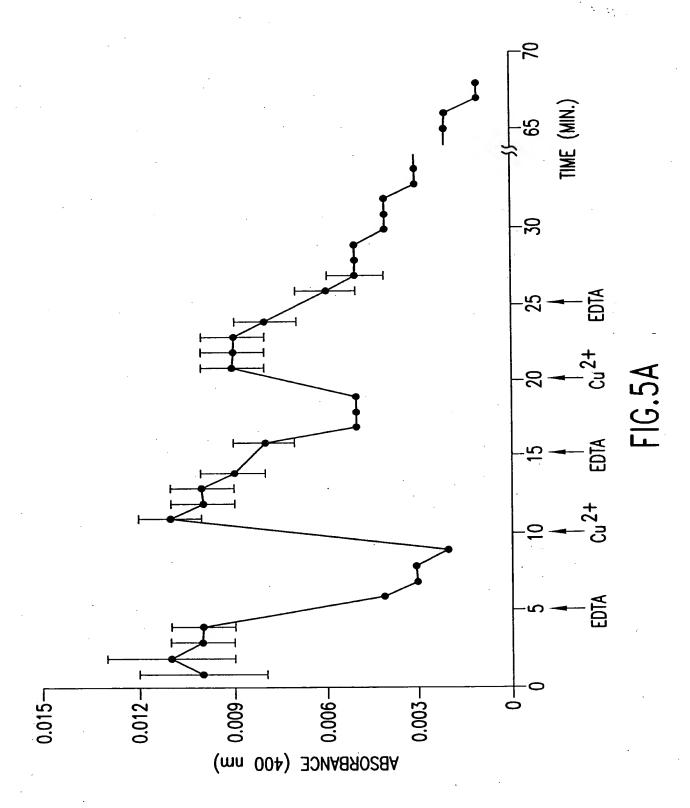
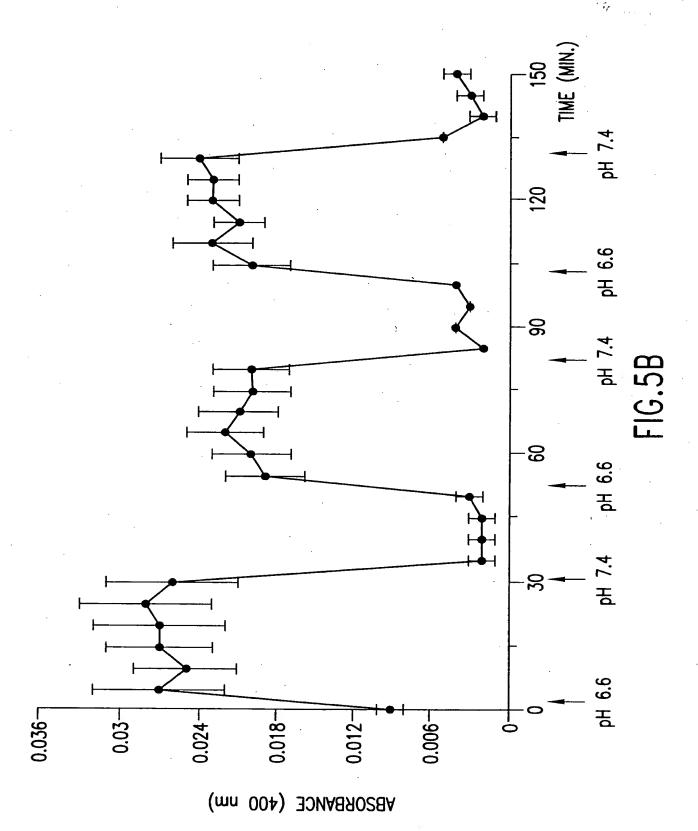


FIG.4C





Sheet 9 of 58

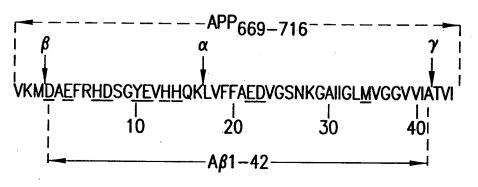
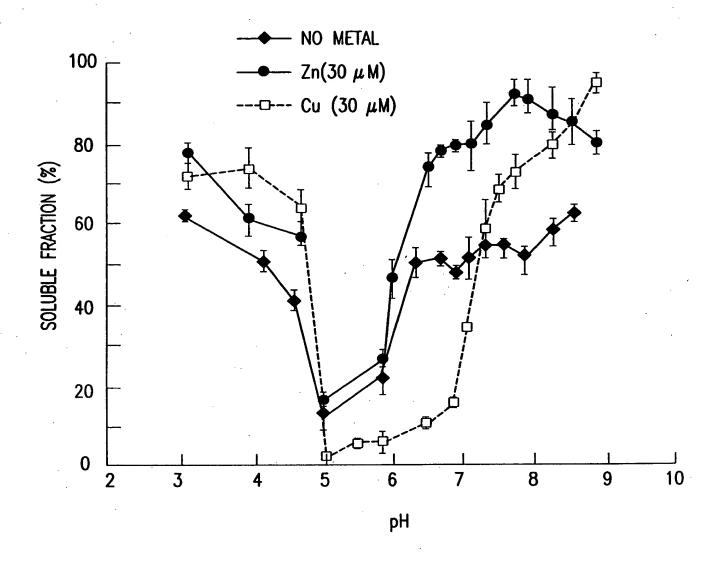


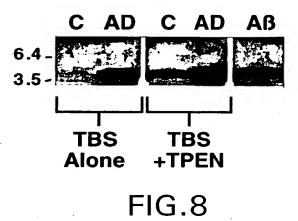
FIG.6



OSESURO OLOUDE

FIG.7

Sheet 12 of 58



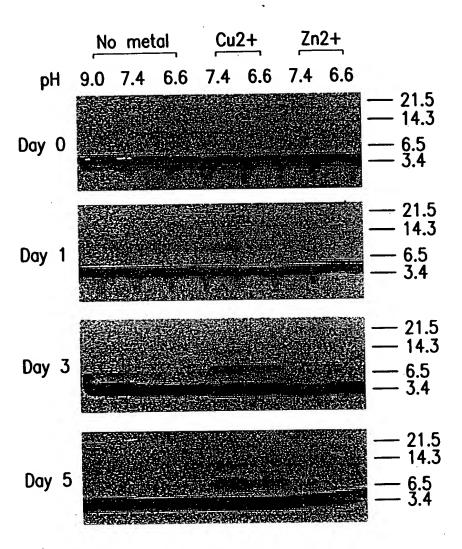
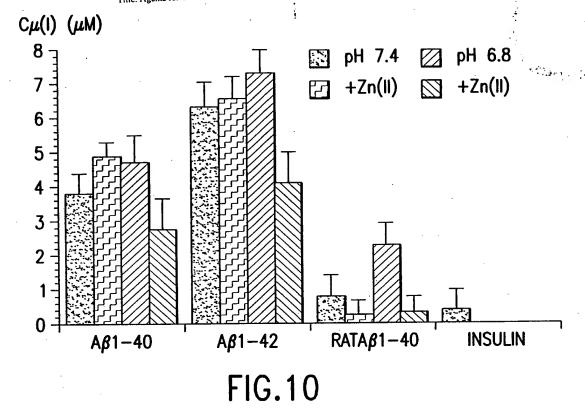
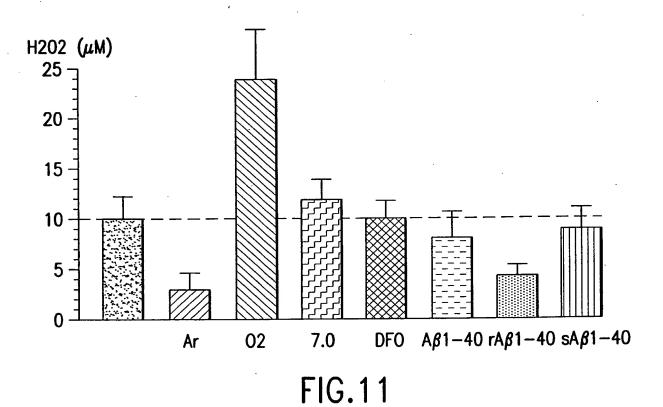


FIG.9





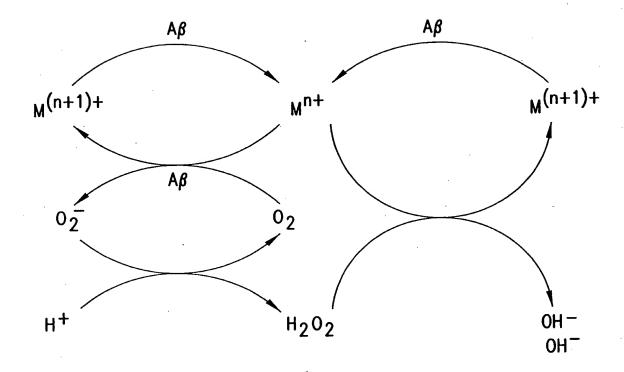


FIG.12

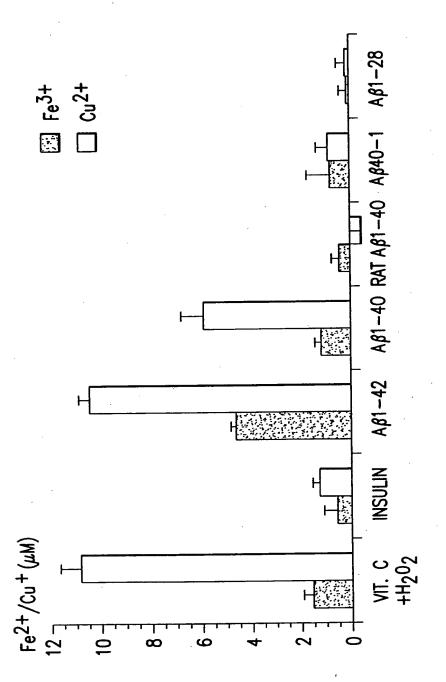


FIG.13A

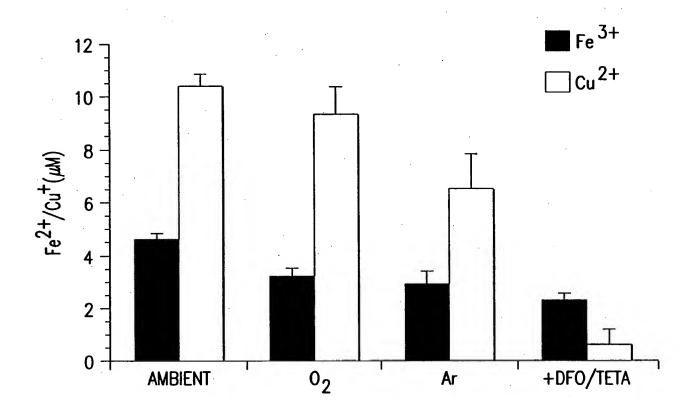


FIG. 13B

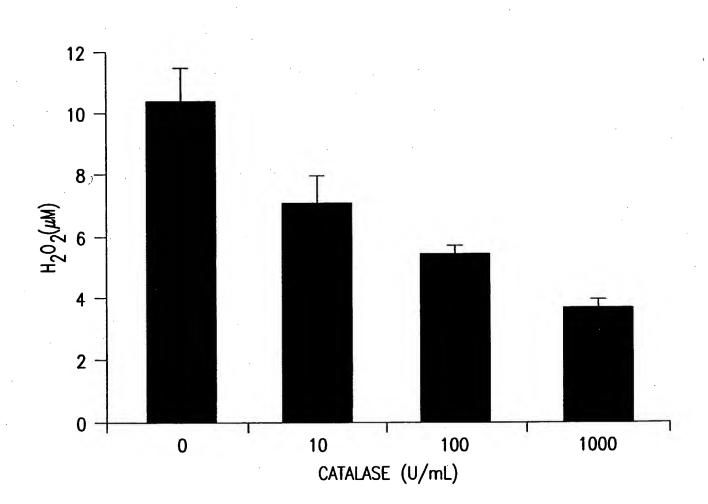


FIG. 14A

tille: Agents for Use in the Treatment of Alzheimer's Diseas

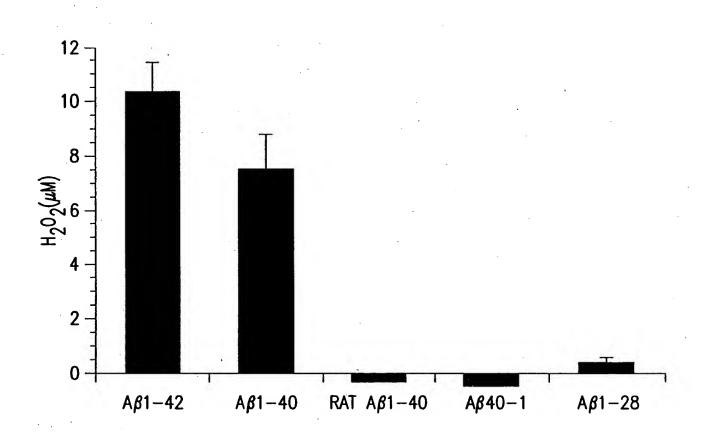


FIG. 14B

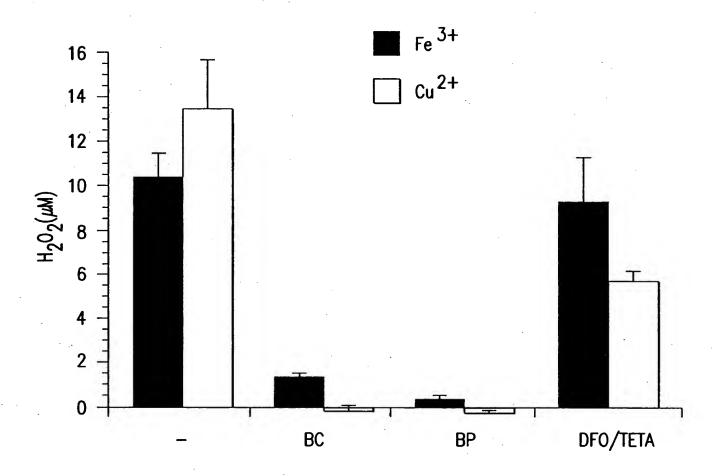


FIG. 14C

Sheet 21 of 58

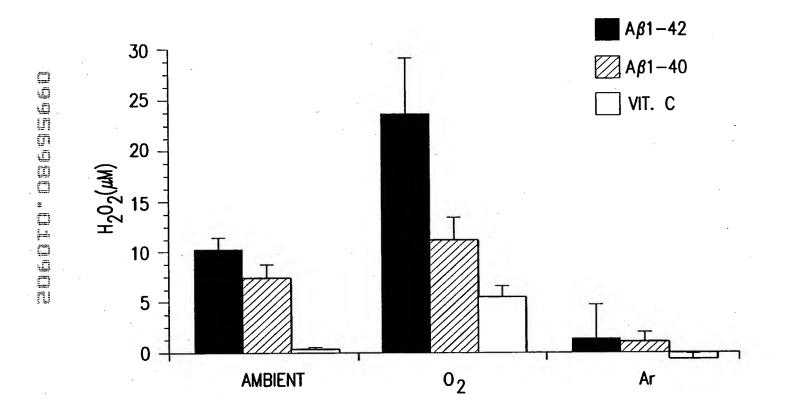


FIG. 14D

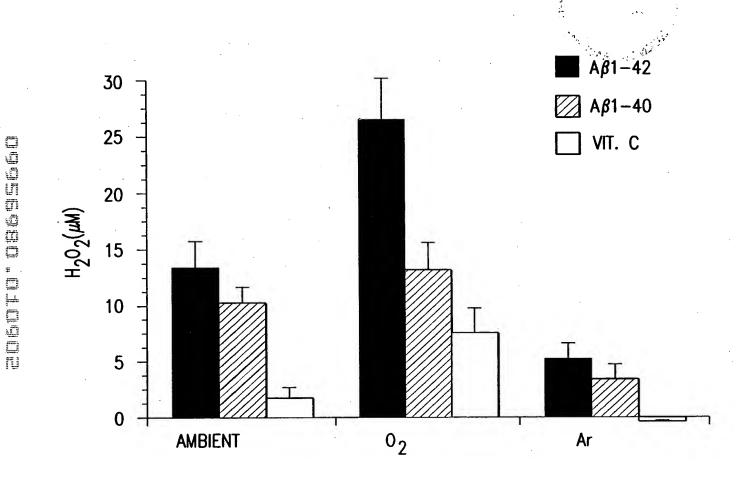


FIG. 14E

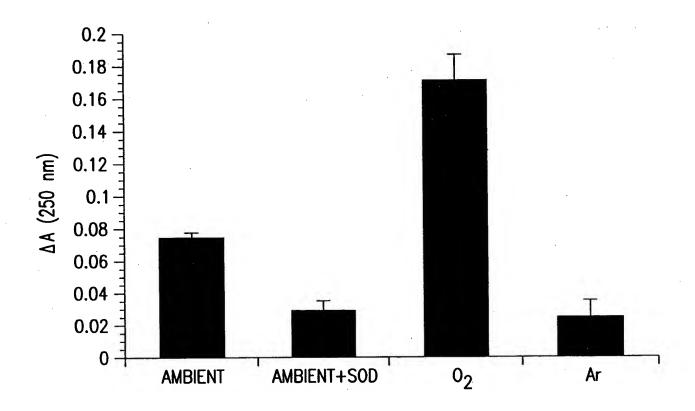


FIG. 15A

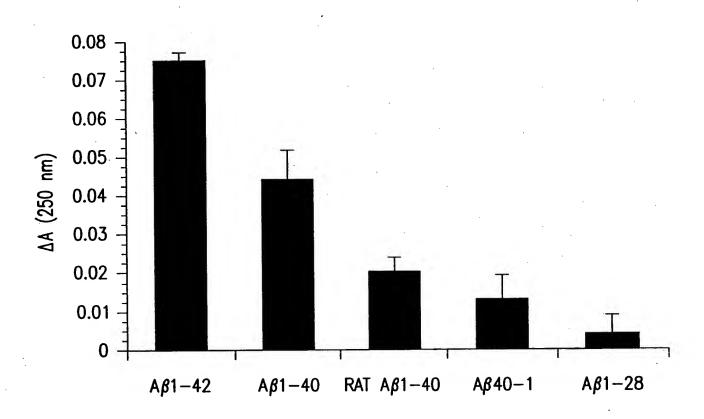
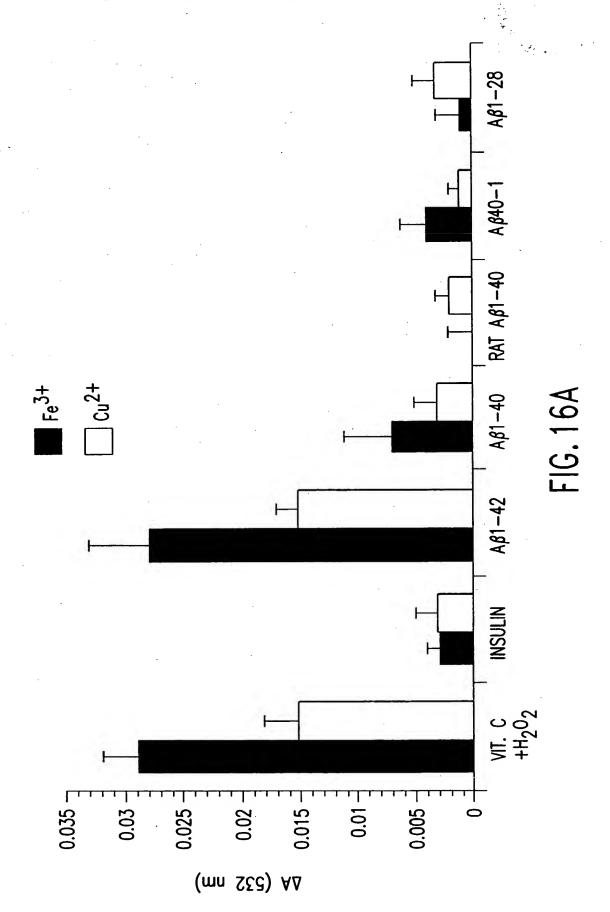
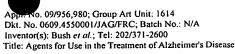


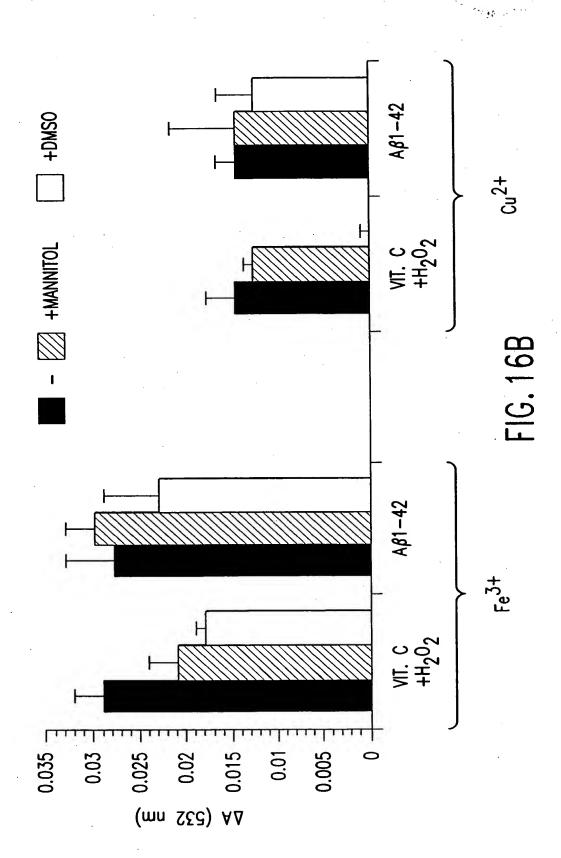
FIG. 15B

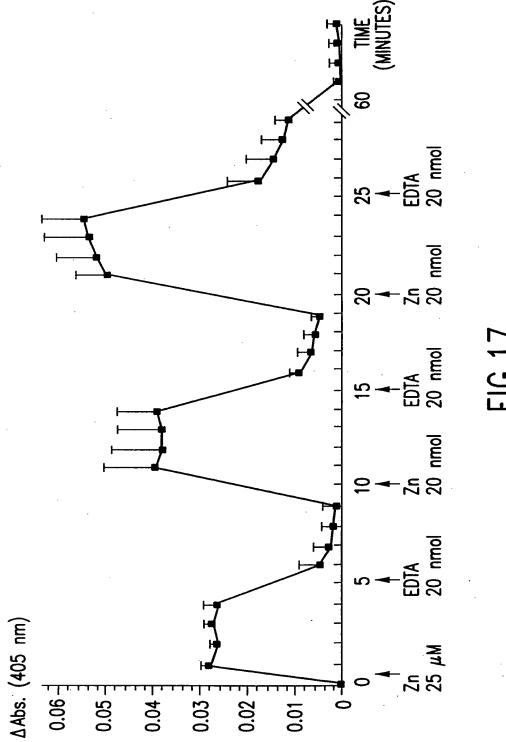
Appl. No. 09/956,980; Group Art Unit: 1614 Dkt. No. 0609.4550001/JAG/FRC; Batch No.: N/A Inventor(s): Bush et al.; Tel: 202/371-2600

Title: Agents for Use in the Treatment of Alzheimer's Disease



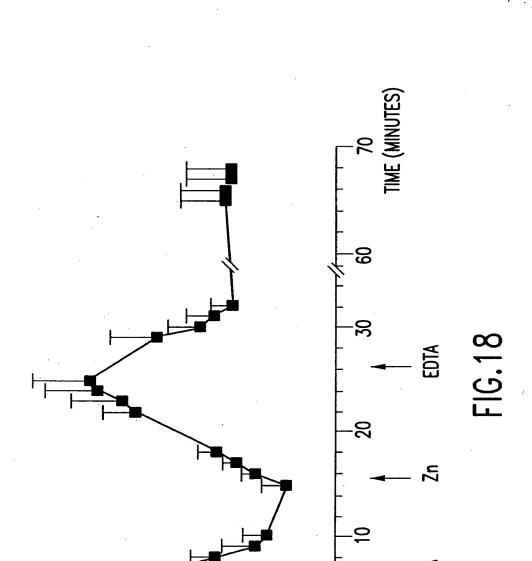


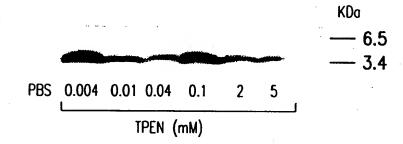




Abs. (400 nm)
0.050
0.045
0.035
0.025
0.020
0.010
0.015

Sheet 28 of 58





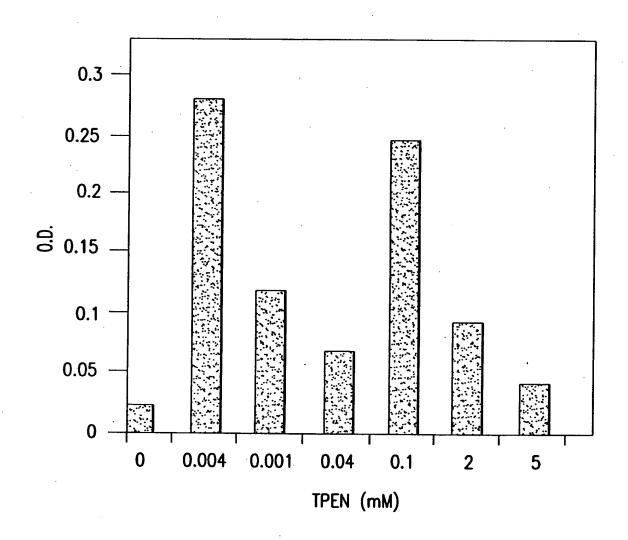
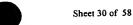
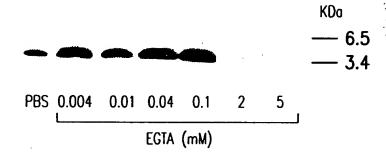


FIG.19A





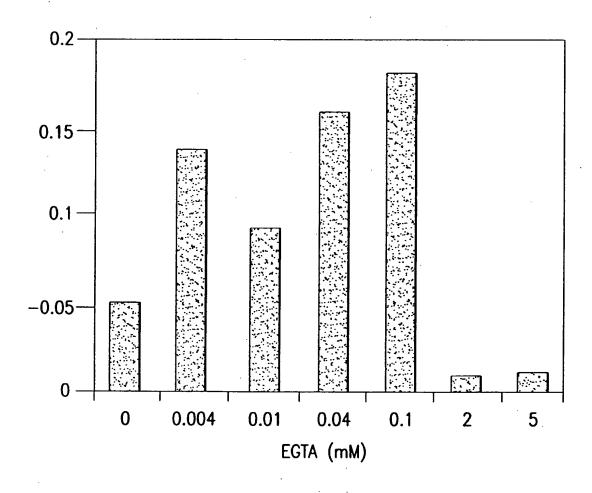
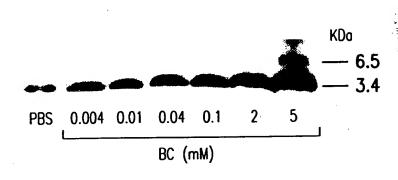


FIG.19B

Appl. No. 09/956,980; Group Art Unit: 1614 Dkt. No. 0609.4550001/JAG/FRC; Batch No.: N/A Inventor(s): Bush et al.; Tel: 202/371-2600

Title: Agents for Use in the Treatment of Alzheimer's Disease



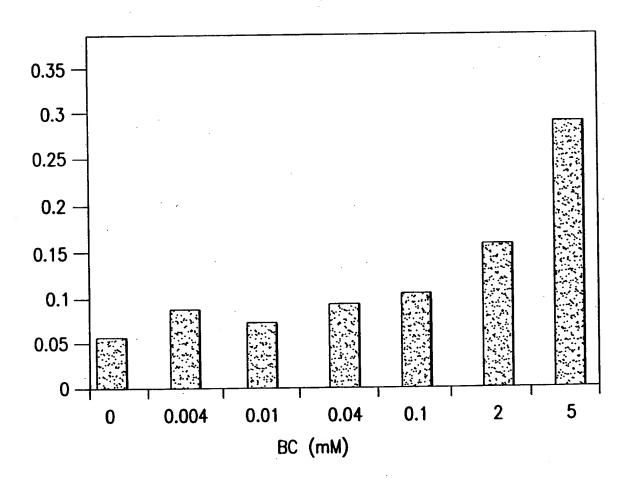
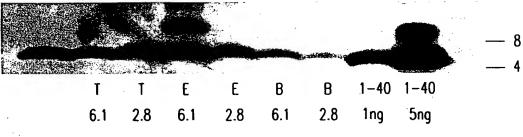


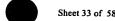
FIG.19C

Sheet 32 of 58

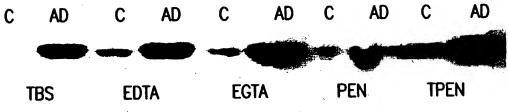


Age- matched control- (indicative gel)

FIG.20A



·



Young control vs AD, various chelators 5mM

FIG.20B

Sheet 34 of 58

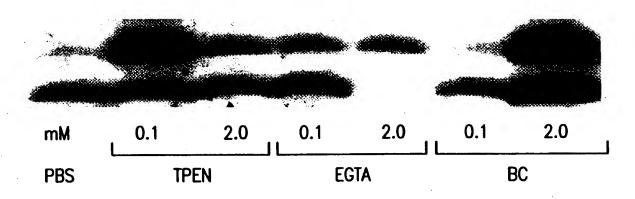
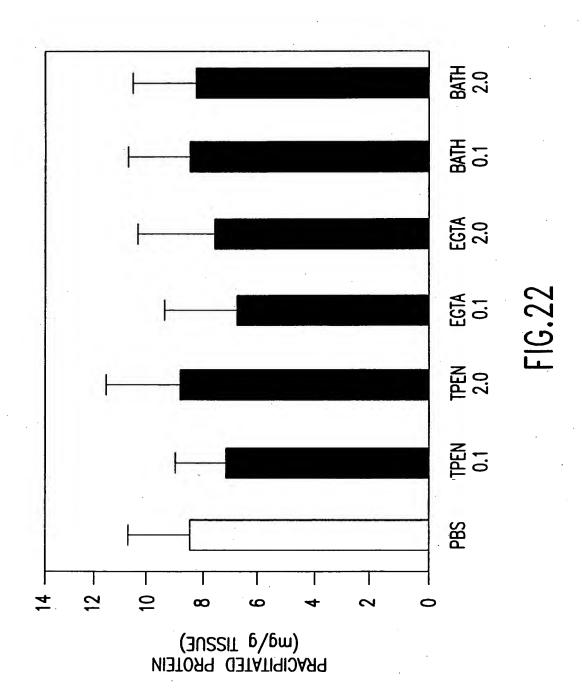
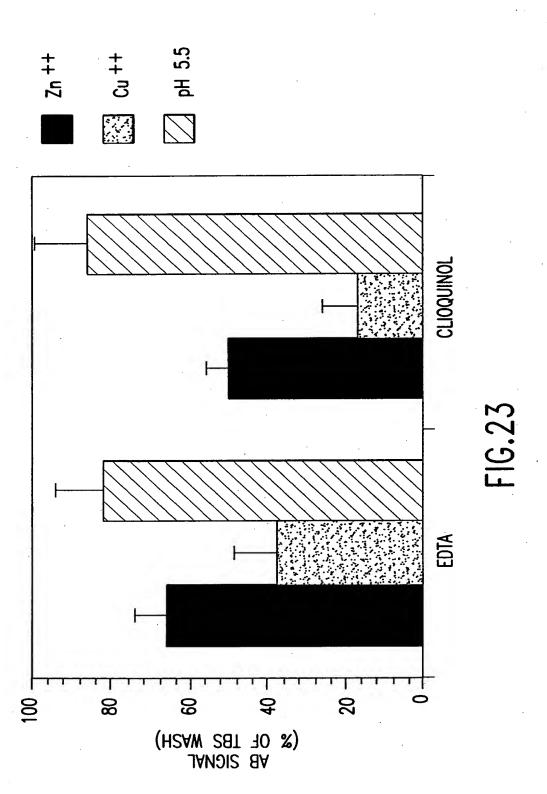


FIG.21





Brain specimen #1



Brain specimen #2

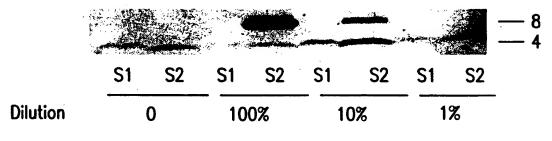
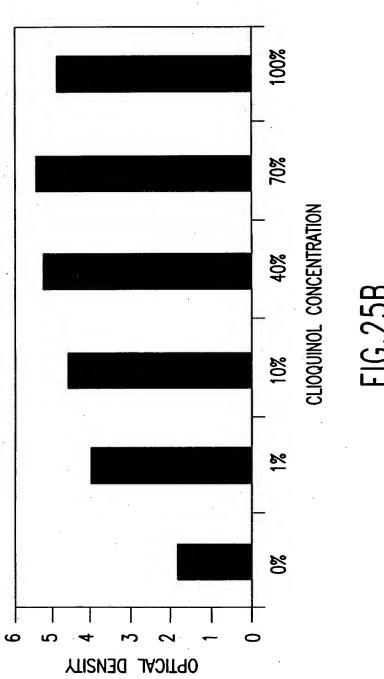


FIG.24

10% 40% 70% 100% 1% **PBS**

`1-40 1-40 0.5ng 2ng

FIG.25A



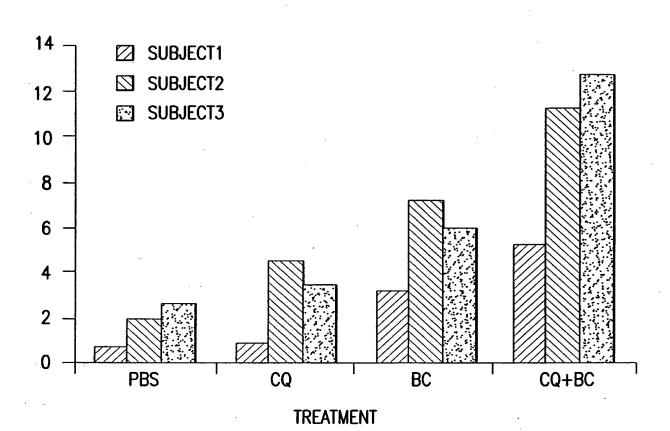
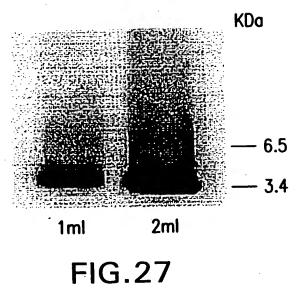
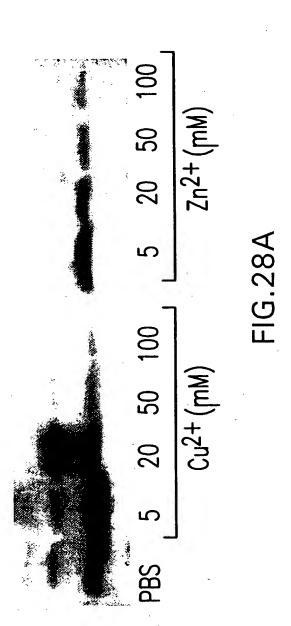


FIG.26

Sheet 41 of 58



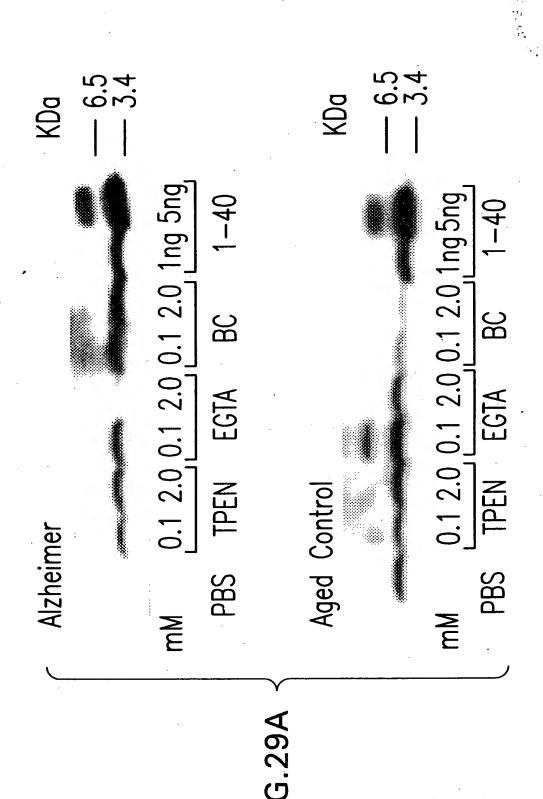
Sheet 42 of 58

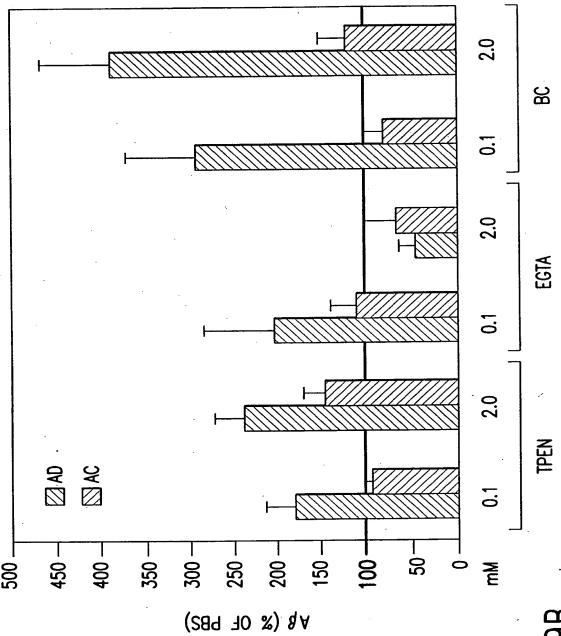


Sheet 43 of 58



PBS Mg²⁺ Ca²⁺ FIG.28B





-16.29B

Sheet 46 of 58

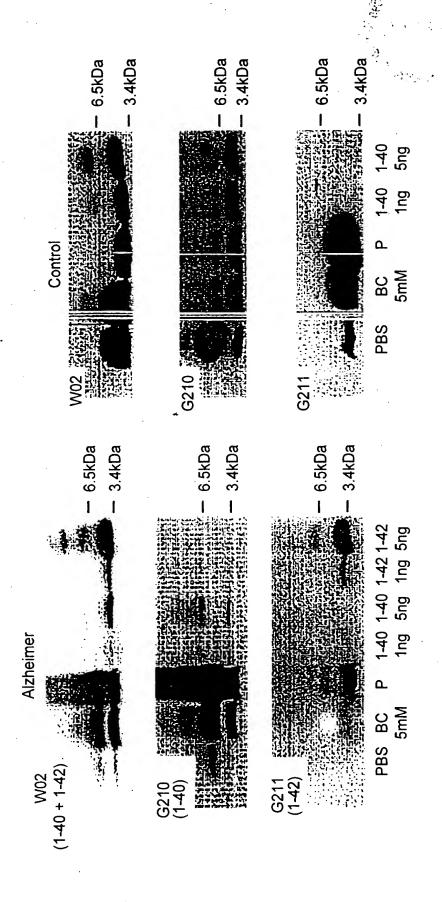
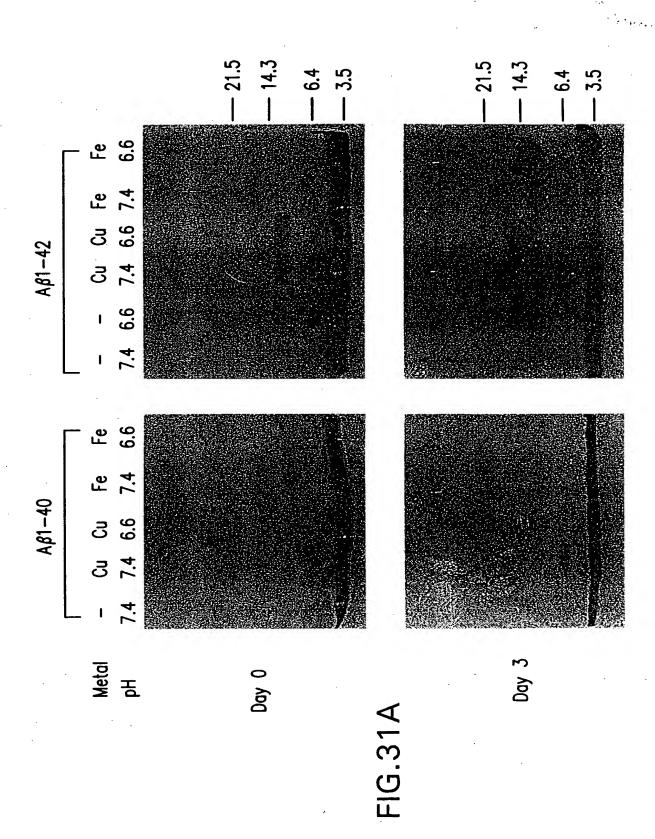
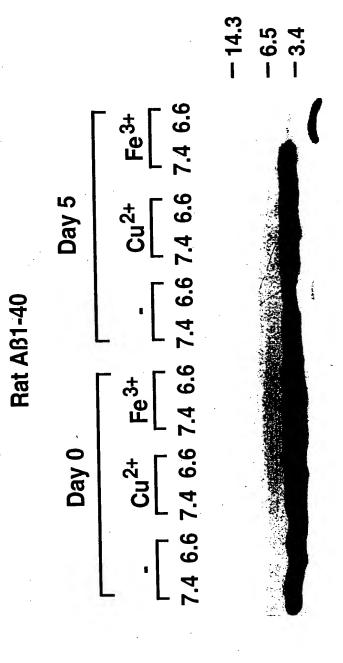


FIG. 30



Sheet 48 of 58



G.31B

 H_2O_2 H_2O_2 - Cu^{2+} Cu^{+} H_2O_2 + Cu^{2+} + Cu^{+} 7.4 6.6 7.4 6.6 7.4 6.6 7.4 6.6 7.4 6.6

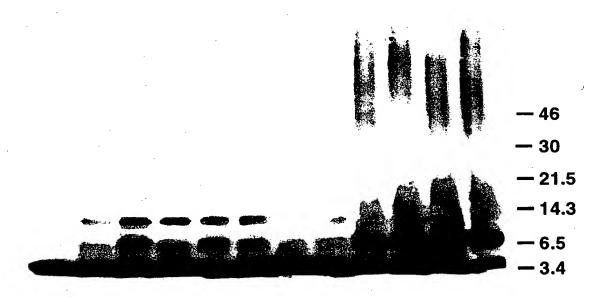


FIG.32A

$$H_2O_2$$
 H_2O_2 H_2O_2

$$- Fe^{3+} Fe^{2+} + Fe^{3+} + Fe^{2+} + Cu^{2+}$$
7.4 6.6 7.4 6.6 7.4 6.6 7.4 6.6 7.4 6.6

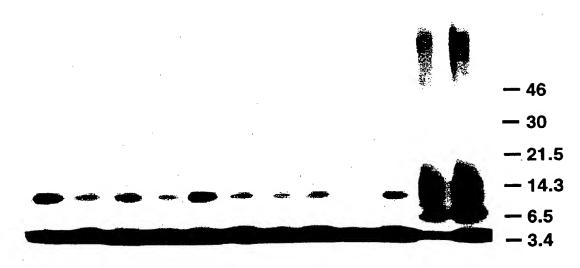


FIG.32B

Sheet 51 of 58

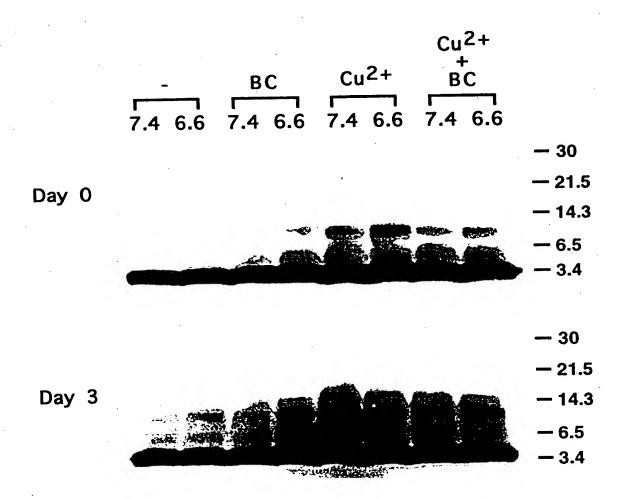


FIG.32C

$$Fe^{2+}$$
 $H_2O_2 +$
 $H_2O_2 \quad Asc. \quad Cu^{2+}$
- $Cu^{2+} \quad Fe^{3+} \quad + Cu^{2+} \quad acid \quad TCEP \quad TCEP$

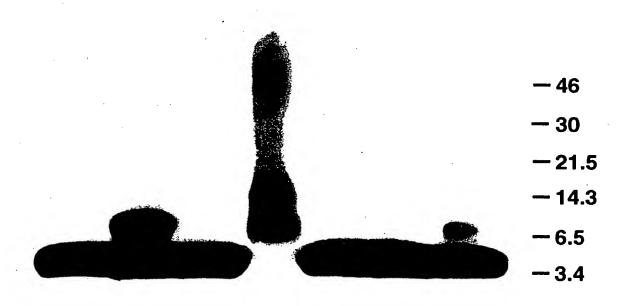


FIG.33A

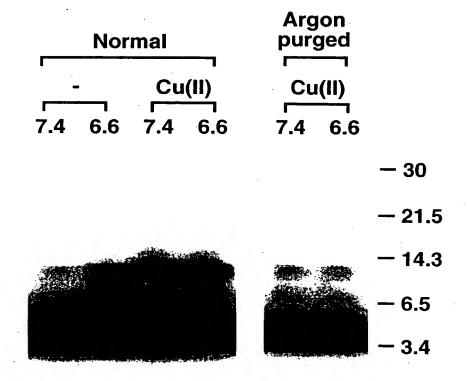
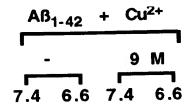


FIG.33B



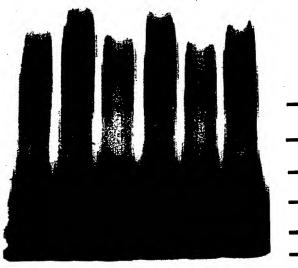


- 46

- 3.4

Urea

FIG.34A



– 46

- 30

- 21.5

— 14.3

-- 6.5

— 3.4

moduno de dinom

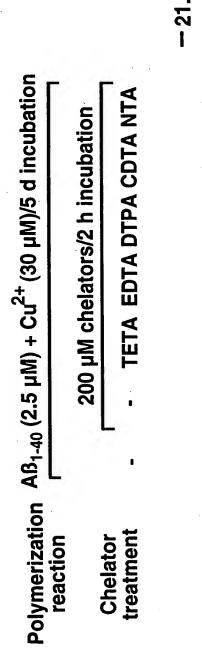


FIG.34B

Polymerization Aβ₁₋₄₂ (2.5 μM) + Cu²⁺ (30 μM)/5 d incubation reaction TETA EDTA DTPA CDTA NTA 200 µМ chelators/2 h incubation Chelator treatment

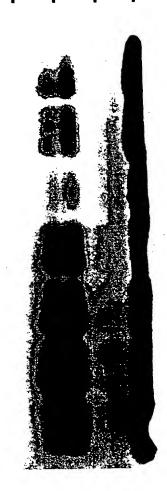


FIG.34C

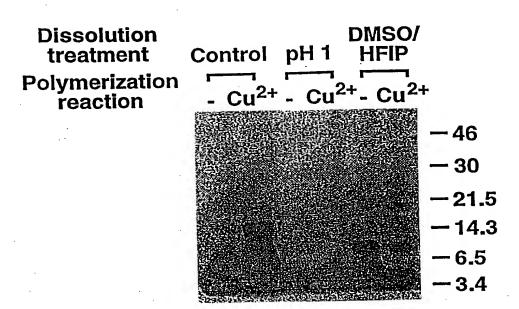


FIG.34D

2 h incubation

Chelator treatment Concentration (mM) TETA TETA BC BC 5 5

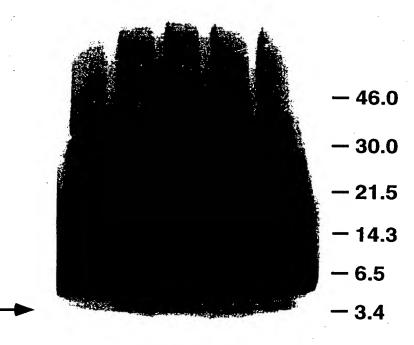


FIG.34E